(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



. I RODIN BONICOO DI EFFERD NON BONIO BONIO BONI ANI NI BONIO BONIO DANI BONIO DELL'ADDO CARL CONTROL DELL'ADD

(43) International Publication Date 14 July 2005 (14.07.2005)

PCT

(10) International Publication Number WO 2005/064021 A3

(51) International Patent Classification:

 C12N 1/21 (2006.01)
 C07K 14/22 (2006.01)

 C12N 15/31 (2006.01)
 C07K 16/12 (2006.01)

 C12N 15/62 (2006.01)
 C07K 14/315 (2006.01)

 C12N 15/63 (2006.01)
 A61K 39/095 (2006.01)

(21) International Application Number:

PCT/EP2004/014770

(22) International Filing Date:

21 December 2004 (21.12.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

0329827.0 23 December 2003 (23.12.2003) GB 0416398.6 22 July 2004 (22.07.2004) GB

- (71) Applicants (for all designated States except US): GLAX-OSMITHKLINE BIOLOGICALS S.A. [BE/BE]; Rue de l'Institut 89, B-1330 Rixensart (BE). UTRECHT UNI-VERSITY [NL/NL]; Padualaan 8, NL-3584 CH Utrecht (NL).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BOS, Martine, Petronella [NL/NL]; Utrecht University, Padualaan 8, NL-3584 CH Utrecht (NL). POOLMAN, Jan [NL/BE]; GlaxoSmithKline Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). TEFSEN, Boris [NL/NL]; Utrecht University, Padualaan 8, NL-3584 CH Utrecht (NL). TOMMASSEN, Johannes, Petrus, Maria [NL/NL]; Utrecht University, Padualaan 8, NL-3584 CH Utrecht (NL).
- (74) Agent: LUBIENSKJ, Michael, John; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and he granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, F1, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP. KE. KG. KP. KR. KZ. LC. LK. LR. LS. LT. LU. LV. MA. MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC. VN. YU. ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA. SD. SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM. AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU. IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID. IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU. LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM. SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW). Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK. TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ. GW, ML, MR, NE, SN, TD, TG)
- of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 23 February 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: VACCINE

(57) Abstract: The present invention discloses a Gram negative bacterium in which the expression of a protein involved in LPS transport to the outer membrane is functionally downregulated such that the level of LPS in the outer membrane is decreased compared to a wild-type Gram negative bacterium. Down regulation of Imp and MsbA proteins can result in such a bacterium. Outer membrane vesicle preparations derived from the Gram negative bacterium of the invention can be used in vaccines to provide protection against bacterial infection.



